

IN THE CLAIMS

1. (Currently Amended) A method of inhibiting mucus secretion by a mucus-secreting cell, comprising administering to said cell a mucus-inhibitory amount of an active fragment of a MARCKS protein that inhibits MARCKS protein-related mucus secretion, wherein said fragment has a sequence comprising from 10 to 50 contiguous amino acids from SEQ ID NO: 3, or an amino acid sequence ~~which is 95% identical to~~ comprising an allelic variant, wherein said variant comprises deletions or replacements in said sequence, wherein said replacements are selected from the group consisting of:

Val or Ser substituted for Ala;

Ala, Leu, Met, or Ile, substituted for Val;

Ala, Val or Ile substituted for Leu;

Pro or Cys substituted for Gly;

Gly, Cys, Ser, or Met substituted for Pro;

Gly, Pro, Ser, or Met substituted for Cys;

Pro or Cys substituted for Met;

Phe or Gln substituted for His;

His, Tyr, or Trp substituted for Phe;

His, Phe or Trp substituted for Tyr;

Phe or Tyr substituted for Trp;

Gln or Ser substituted for Asn;

His, Lys, Glu, Asn, or Ser substituted for Gln;

Gln, Thr, Pro, Cys or Ala substituted for Ser;

Gln or Ser substituted for Thr;

Gln or Arg substituted for Lys;

Lys, Asp or Glu substituted for Arg

Lys, Arg, or Glu substituted for Asp;

Arg or Asp substituted for Glu; and

combinations of any of the foregoing; and

whereby mucus secretion by said cell is reduced compared to that which would occur in the absence of said active fragment.

2-5. (Canceled).

6. (Previously Presented) A method according to claim 1 wherein said method further comprises administering a compound selected from the group consisting of okadaic acid, calphostin C, Rp-8-Br-cGMP and LY83583.

7. (Original) A method according to claim 1 wherein said mucus-secreting cell is an epithelial cell contained within airway mucous membranes or gastrointestinal mucous membranes.

8. (Original) A method according to claim 1, wherein said compound is administered to the airways of a mammalian subject.

9. (Original) A method according to claim 1, wherein said compound is administered to the gastrointestinal tract of a mammalian subject.

10. (Original) A method according to claim 1 wherein said compound is administered by inhalation.

11. (Currently Amended) A method of inhibiting mucus secretion by a mucus-secreting cell, comprising administering to said cell a peptide inhibitor of MARCKS-related mucus secretion, wherein said peptide inhibitor is selected from the group consisting of

(a) SEQ ID NO: 1;

(b) an active fragment of a MARCKS protein comprising from 10 to 50 contiguous amino acids from SEQ ID NO:3; and

(c) an amino acid sequence ~~which is 95% identical to~~ comprising an allelic variant, wherein said variant comprises deletions or replacements in the sequence of
(a) or (b) above, wherein said replacements are selected from the group consisting of:

Val or Ser substituted for Ala;

Ala, Leu, Met, or Ile, substituted for Val;

Ala, Val or Ile substituted for Leu;
Pro or Cys substituted for Gly;
Gly, Cys, Ser, or Met substituted for Pro;
Gly, Pro, Ser, or Met substituted for Cys;
Pro or Cys substituted for Met;
Phe or Gln substituted for His;
His, Tyr, or Trp substituted for Phe;
His, Phe or Trp substituted for Tyr;
Phe or Tyr substituted for Trp;
Gln or Ser substituted for Asn;
His, Lys, Glu, Asn, or Ser substituted for Gln;
Gln, Thr, Pro, Cys or Ala substituted for Ser;
Gln or Ser substituted for Thr;
Gln or Arg substituted for Lys;
Lys, Asp or Glu substituted for Arg
Lys, Arg, or Glu substituted for Asp;
Arg or Asp substituted for Glu; and
combinations of any of the foregoing;

such that mucus secretion by said cell is inhibited compared to that which would occur in the absence of said peptide.

12-13. (Canceled).

14. (Original) A method according to claim 11 wherein said mucus-secreting cell is an epithelial cell contained within airway mucous membranes or gastrointestinal mucous membranes.

15. (Original) A method according to claim 11, wherein said peptide is administered to the airways of a mammalian subject.

16. (Original) A method according to claim 11, wherein said peptide is administered to the gastrointestinal tract of a mammalian subject.

17. (Original) A method according to claim 15 wherein said peptide is administered by inhalation.

18. (Currently Amended) A method of inhibiting mucus secretion in the airways of a subject in need of such treatment, comprising administering to the airways of said subject a mucus-inhibiting amount of a compound that inhibits the MARCKS-related release of mucin, wherein said compound is selected from the group consisting of

(a) SEQ ID NO: 1;

(b) an active fragment of a MARCKS protein comprising from 10 to 50 contiguous amino acids from SEQ ID NO:3;

(c) an amino acid sequence ~~which is 95% identical to~~ comprising an allelic variant, wherein said variant comprises deletions or replacements in the sequence of
(a) or (b) above, wherein said replacements are selected from the group consisting of:

Val or Ser substituted for Ala;

Ala, Leu, Met, or Ile, substituted for Val;

Ala, Val or Ile substituted for Leu;

Pro or Cys substituted for Gly;

Gly, Cys, Ser, or Met substituted for Pro;

Gly, Pro, Ser, or Met substituted for Cys;

Pro or Cys substituted for Met;

Phe or Gln substituted for His;

His, Tyr, or Trp substituted for Phe;

His, Phe or Trp substituted for Tyr;

Phe or Tyr substituted for Trp;

Gln or Ser substituted for Asn;

His, Lys, Glu, Asn, or Ser substituted for Gln;

Gln, Thr, Pro, Cys or Ala substituted for Ser;

Gln or Ser substituted for Thr;

Gln or Arg substituted for Lys;

Lys, Asp or Glu substituted for Arg

Lys, Arg, or Glu substituted for Asp;
Arg or Asp substituted for Glu; and
combinations of any of the foregoing; and
whereby mucus secretion in the airways of the subject is reduced compared to that which would occur in the absence of said treatment.

19. (Original) A method according to claim 18 wherein said subject is a mammalian subject suffering from a condition selected from the group consisting of bronchitis, asthma, cystic fibrosis, chronic obstructive pulmonary disease, emphysema, pneumonia, influenza, rhinitis and the common cold.

20-23. (Canceled).

24. (Previously Presented) A method according to claim 18, further comprising administering a compound selected from the group consisting of okadaic acid, calphostin C, Rp-8-Br-cGMP) and LY83583.

25. (Original) A method according to claim 18 wherein said compound is administered by inhalation.

26-38 (Cancelled).

39. (Currently Amended) A pharmaceutical formulation comprising a mucus-inhibiting peptide fragment of MARCKS, wherein said mucus-inhibiting peptide fragment is selected from the group consisting of

- (a) SEQ ID NO: 1;
- (b) an active fragment of a MARCKS protein comprising from 10 to 50 contiguous amino acids from SEQ ID NO:3; and
- (c) an amino acid sequence ~~which is 95% identical to~~ comprising an allelic variant, wherein said variant comprises deletions or replacements in the sequence of (a) or (b) above, wherein said replacements are selected from the group consisting of:
Val or Ser substituted for Ala;

Ala, Leu, Met, or Ile, substituted for Val;
Ala, Val or Ile substituted for Leu;
Pro or Cys substituted for Gly;
Gly, Cys, Ser, or Met substituted for Pro;
Gly, Pro, Ser, or Met substituted for Cys;
Pro or Cys substituted for Met;
Phe or Gln substituted for His;
His, Tyr, or Trp substituted for Phe;
His, Phe or Trp substituted for Tyr;
Phe or Tyr substituted for Trp;
Gln or Ser substituted for Asn;
His, Lys, Glu, Asn, or Ser substituted for Gln;
Gln, Thr, Pro, Cys or Ala substituted for Ser;
Gln or Ser substituted for Thr;
Gln or Arg substituted for Lys;
Lys, Asp or Glu substituted for Arg
Lys, Arg, or Glu substituted for Asp;
Arg or Asp substituted for Glu; and
combinations of any of the foregoing; and
a pharmaceutically acceptable carrier.

40-41. (Canceled).

42. (Original) A pharmaceutical formulation according to claim 39 where said composition is aerosolized.

43. (Original) A pharmaceutical formulation according to claim 39 where said peptides are contained within liposomes.

44-47. (Canceled).

48. (Currently Amended) A method of inhibiting mucus secretion by a mucus-secreting cell, comprising administering to said cell a mucus-inhibitory amount of a compound, wherein said compound is a peptide having an amino acid sequence that comprises from 10 to 50 contiguous amino acids from an N-terminal sequence of a MARCKS protein or an amino acid ~~which is 95% identical to~~ sequence comprising an allelic variant, wherein said variant comprises deletions or replacements in said sequence that binds to a target site selected from:

- (a) mucin granule membranes at the site bound by MARCKS protein; and
- (b) MARCKS protein at the mucin granule binding site; and

wherein said replacement is selected from the group consisting of:

Val or Ser substituted for Ala;

Ala, Leu, Met, or Ile, substituted for Val;

Ala, Val or Ile substituted for Leu;

Pro or Cys substituted for Gly;

Gly, Cys, Ser, or Met substituted for Pro;

Gly, Pro, Ser, or Met substituted for Cys;

Pro or Cys substituted for Met;

Phe or Gln substituted for His;

His, Tyr, or Trp substituted for Phe;

His, Phe or Trp substituted for Tyr;

Phe or Tyr substituted for Trp;

Gln or Ser substituted for Asn;

His, Lys, Glu, Asn, or Ser substituted for Gln;

Gln, Thr, Pro, Cys or Ala substituted for Ser;

Gln or Ser substituted for Thr;

Gln or Arg substituted for Lys;

Lys, Asp or Glu substituted for Arg

Lys, Arg, or Glu substituted for Asp;

Arg or Asp substituted for Glu; and

combinations of any of the foregoing;

wherein the amount of mucus secreted by said cell is reduced compared to that which would occur in the absence of said compound.

49. (Canceled).

50. (Previously Presented) A method according to claim 49 48 where said peptide is myristoylated.

51-66 (Cancelled).

67. (Previously Presented) The method of Claim 1, wherein the N-terminal region of the active fragment of a MARCKS protein is myristoylated.

68. (Previously Presented) The method of Claim 1, wherein said active fragment of a MARCKS protein corresponds to the myristoylated N-terminus of MARCKS.

69. (Previously Presented) The method of Claim 1, wherein said active fragment of a MARCKS protein comprises SEQ ID NO: 1.

70. (Previously Presented) The method of Claim 18, wherein the N-terminal region of the active fragment of a MARCKS protein is myristoylated.

71. (Previously Presented) The method of Claim 18, wherein said active fragment of a MARCKS protein corresponds to the myristoylated N-terminus of MARCKS.

72. (Previously Presented) The method of Claim 39, wherein the N-terminal region of the active fragment of a MARCKS protein is myristoylated.

73. (Previously Presented) The method of Claim 39, wherein said active fragment of a MARCKS protein corresponds to the myristoylated N-terminus of MARCKS.

74. (Previously Presented) The method of Claim 48, wherein the N-terminal region of the active fragment of a MARCKS protein is myristoylated.

75. (Previously Presented) The method of Claim 48, wherein said active fragment of a MARCKS protein corresponds to the myristoylated N-terminus of MARCKS.

76. (Previously Presented) A method of inhibiting mucus secretion by a mucus-secreting cell, comprising administering to said cell a peptide inhibitor of MARCKS-related mucus secretion, wherein said peptide inhibitor comprises SEQ ID NO: 1.